S246 Renal transplantation and infection—focus on CMV

V.C. Emery. *Royal Free and University College Medical School, London, UK*

CMV is a continuing cause of morbidity in the renal transplant recipient. As more high-risk transplantation is performed due to lack of suitably matched organs, the incidence of CMV infection is increasing. My talk will focus on the insight that CMV load measures can provide in understanding the pathogenesis of CMV disease and the interrelationship between viral load in the blood and urine and established risk factors for CMV disease such as donor/recipient CMV serostatus, augmented immunosuppression, etc. A series of investigations in my laboratory has shown, using quantitative PCR methods, that CMV load is the most important parameter in CMV pathogenesis and accounts for the previous risk factors. The utility of these data in the context of antiviral intervention will then be discussed—how effective therapy needs to be to suppress replication and impact on disease, and the benefits/drawbacks of pre-emptive versus prophylactic regimens. I will conclude by discussing recent data implicating HHV-7 as a cofactor for CMV disease in renal transplant recipients and the possibility that controlled clinical trials aimed at inhibiting CMV replication may produce beneficial effects through inhibition of other beta-herpesviruses.

S247 Infections in ICU patients: focus on resistant bacteria

J. Chastre. *Réanimation Médicale, Hôpital Bichat, Paris, France*

The importance of multiresistant microorganisms as a cause of nosocomial infection in ICU patients has been documented in many studies. By now, many *Pseudomonas aeruginosa* and *Acinetobacter baumannii* strains are class I cephalosporinase producers and are resistant to piperacillin, aztreonam and ceftazidime. *Klebsiella pneumoniae* strains are also increasingly recognized as producers of transferable extended-spectrum beta-lactamases which confer resistance to third-generation cephalosporins. Other multiresistant aerobic Gram-negative bacilli include *Xanthomonas (Stenotrophomonas) maltophilia* and *alcaligenes*. Unfortunately, methicillin-resistant *Staphylococcus aureus* is also more and more frequently implicated as a causative pathogen in very sick patients who require ICU care for a long period of time. Therefore, the microbiological trends in nosocomial infection are evolving towards more resistant and more difficult-to-treat pathogens. A large body of evidence strongly supports the observation that the indiscriminate use of antimicrobial agents in ICU patients has immediate but also long-term consequences, contributing to the emergence of multiresistant pathogens and increasing the risk of serious superinfections. Virtually all reports emphasize that better antibiotic control programs in order to limit bacterial resistance are urgently needed in ICUs and that patients without true infection should not receive antimicrobial treatment. Therefore, it should be made clear to physicians confronted with ICU patients clinically suspected of having developed nosocomial infection that treating all these patients with new antimicrobial agents may lead to overtreatment in a large number of cases and, thus, to the rapid emergence of multiresistant pathogens not only in the treated patients but also in other patients hospitalized in the same unit.

Pharmacoeconomics in infectious diseases

S252 Outcome modeling in infectious diseases

A. Brandt. *Institute for Medical Informatics and Biostatistics, Riehen, Switzerland*

Medical economic evaluations have been performed for many pharmaceutical substances and immunization programs. Study results have helped to improve health policy decisions regarding preventive immunization and acute treatment. Disease models are used to estimate the medical outcomes and cost consequences of alternative intervention strategies, not just pharmaceutical treatments. Studies indicate that primary prevention is often more efficient in high-risk rather than low-risk populations and that secondary prevention tends to be more efficient than primary prevention.

The evaluation of alternative antimicrobial treatments requires answers to a sequence of questions: Who needs treatment? How is the target population defined? What are the best treatments, doses, routes of administration, and duration of treatment? How can the expected long-term medical outcomes be estimated for a given target population, particularly in the face of only short-term evidence? What are the expected cost consequences of alternative treatments?

Disease models attempt to represent disease processes, based on a synthesis of available medical data. They simulate the development of diseases for different patient populations under different management strategies: extrapolate short-term data and surrogate endpoints to long-term clinical outcomes; extrapolate from trial data to population (efficacy to effectiveness) in clinical practice; what-if analyses of different assumptions. Additionally, disease models allow us to determine the most important efficiency parameter as well as cost parameter by sensitivity analysis as well as to direct scarce resources to efficient treatments.

Infections by non-tuberculous mycobacteria

S253 Infections by non-tuberculous mycobacteria

J. Falkinham, *Virginia State University, Fralin Biotechnology Center, Blacksburg, VA, USA*

Non-tuberculous mycobacteria are opportunistic, intracellular pathogens whose source is environmental. Infection is associated with predisposing conditions: lung disease, alteration in chest architecture, or immune deficiency. Lung, skin, lymph node, gastrointestinal, disseminated and nosocomial infections have been reported.

Examples of non-tuberculous mycobacteria causing pulmonary infections include *Mycobacterium kansasii*, *M. avium*, *M. intracellulare*, *M. malmoense* and *M. xenopi*. Though the epidemiologies of the infections differ, *M. marinum*, *M. haemophilum* and *M. ulcerans* have all been implicated in skin infections. *M. avium* is responsible cervical lymphadenitis in children. *M. paratuberculosis* causes diarrheal disease (Johne's) in cattle and may be responsible for Crohn's disease in humans. Although the majority of disseminated infections in AIDS patients are caused by *M. avium*, other mycobacterial species, including *M. kansasii*, *M. malmoense* and newly identified species (e.g. *M. genavense*), are responsible for infection as well.

One source of non-tuberculous mycobacterial infection is water. *M. avium* isolates from water have DNA fingerprints matching those of isolates from either human AIDS patients or SIV-infected monkeys who drank the water. Outbreaks of *M. xenopi* and *M. ulerans* have been associated, in time, with recovery from hot water systems or the